The Epitrichial Layer of the Epidermis and its Relationship to Ichthyosis Congenita.

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REPRINTED FROM THE

JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES

FOR DECEMBER, 1895.

[Reprinted from the JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES for December, 1895.]

THE EPITRICHIAL LAYER OF THE EPIDERMIS AND ITS RELATIONSHIP TO ICHTHYOSIS CONGENITA.*

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IT is my object in this brief communication to call the notice of the association to a well-marked layer of cells found in the epidermis of young embryos, which has been observed and described as forming a distinct membrane covering the hairs in certain of the lower animals. Welcker, of Halle, was the first to describe this layer. He found in an embryo of a sloth a distinct outer membrane covering the hair development of the animal. To this he gave the name *epitrichium*, on account of its position overlying the hairs. He further found that this existed as a distinct membrane in certain mammals, while in others, where there was no separable membrane, the upper cells of the ectoderm were different histologically from the cells below.

He reserves the name *epitrichium*, therefore, for the separable membrane found only in certain mammals; the outer layer of histologically distinct cells found in certain other mammals, and evidently homologous with the epitrichium, is called the *epitrichial layer*. In man, he describes distinctly an epitrichial layer, consisting of large cells with round nuclei much larger than those of the epidermal layers beneath.

This *epitrichial layer* in man has not received recognition. Kölliker states that it is not proved that there is a distinct difference histologically between the outer cells and those beneath, nor that it is these

* Read at the nineteenth annual meeting of the American Dermatological Association, Montreal, Canada, September, 1895.

outer cells alone that are cast off. Welcker's *epitrichium*, however, meaning by this the distinctly separable membrane of certain animals, has been generally accepted.

My attention was directed to this subject in 1887 by Dr. C. S. Minot, who had seen in shreds of fœtal skin, when stained by carmine or hæmatoxylin and examined with outer surface uppermost, a layer of large cells of polygonal form with a granular body in the center, and within this a nucleolus. He considered these cells to be part of the epitrichial layer described by Welcker in 1864, and since forgotten.

During the following two years I spent much time in investigating this question, and the results of my work were embodied in an article in the *Anatomischer Anzeiger* for 1889. As this journal is one not commonly read by dermatologists unless especially interested in some anatomical subject, and as I think the persistence of this epitrichial layer may play some part in the ætiology of certain affections of the skin, I take the liberty of briefly reviewing some of the conclusions that I arrived at in the article referred to.

It was found that in embryos of from two to three months, the epidermis possessed an outermost layer of large polygonal cells, granular in appearance and with large nuclei. Moreover, the shape of these cells was peculiar, many of them having a rounded, puffed-out, or "domed" appearance. These cells I considered to be the outermost layer of polygonal cells that are seen in the two-celled period of epidermal development, these outer cells persisting and becoming transformed into the domed cells, while beneath them the other mucous layers are formed. In embryos of from three to four months there were seen two rows of outer granular cells, many of them having a puffed-out, bladderlike appearance, so that they may be called bladder cells. A very large number of embryos (fifty at the least) were examined for these cells, and bits of skin were taken from many different parts of the body. In all parts these peculiar cells were found. They were more numerous in the best preserved specimens and when the sections were carefully handled. It was found that in the sixth month this layer had disappeared over most parts of the body.

It was held that there were good reasons for considering these cells as forming a definite and distinct histological layer. They differed greatly in size, form, and general appearance from the cells of the mucous layers below. They were very unlike the cells of the later horny layer, which is produced solely from the mucous layer, the epitrichial layer, at least on most parts of the body, not being concerned in its production. When the horny layer has made its appearance, the epitrichial layer has disappeared, with the exception of a few clumps

of bladder cells seen sticking to the scales. The close resemblance of this layer of cells to the elements comprising the epitrichium that covers the hair of certain animals and the epitrichial layer of certain other animals, points forcibly to the conclusion that they are homologous structures. Moreover, the partially horny tissue that covers the fœtal nail, and that has been named by Unna the *eponychium*, is evidently a part of the epitrichial layer, as one can trace a direct connection between the eponychium and the domed and bladder cells that have been described. In embryos of five months, after the nail has become exposed by the loss of the epitrichial layer over most of the surface, a heaping up of horny cells is found at the nail edge, forming a thick ridge. This is produced by a persistence of the epitrichial layer at this point and by a keratosis of the bladder cells; the horny formation not, in my opinion, being derived from the mucous layers, as is the stratum corneum.

At the time these investigations were made my attention was naturally directed to the question whether any known epidermal anomalies were to be explained by the persistence of the epitrichial layer after birth, and the class of cases that has been described under the title of "ichthyosis congenita" suggested themselves at the outset. No example of this condition had, however, fallen under my observation, and the cases reported varied so greatly in degree, and were so variously interpreted by different writers, that speculation as to their ætiology seemed worse than useless. In the summer of 1892, however, a case was brought to me that at once suggested the persistence of this embryonic epitrichial layer at the time of birth. The patient was a male, seven months of age. The skin of the trunk, legs, and arms was thickened slightly, and scaling moderately in rather large flakes, especially upon the back. The skin of the legs was comparatively normal. There was considerable scaling and thickening of the scalp, especially of the occiput. The father and mother were both healthy, and had previously had five healthy children, and no family history of importance could be elicited. The parents' account of the condition of the child's skin at birth was corroborated by the physician who had been in attendance, Dr. Bacon, of Brockton. Dr. Bacon said that when the child was born there seemed to be a thin, perfectly smooth membrane covering it completely from head to foot, which was not detached, but closely adherent to the underlying tissues. In smoothness and in appearance this membrane suggested paraffin paper. It was five weeks before much of this membrane was lost, when it began to peel off in large strips—not in the form of branny scales. The skin underneath the membrane looked normal, but a process of slow scaling had been

going on after the membrane had peeled off, which was diminishing gradually when the patient was seen by me. According to the attending physician, there had been no ectropion, and no deep fissures and cracks in the skin such as are described in many recorded cases of ichthyosis congenita.

It was afterward learned that the child died of diphtheria in January, 1893, and that before the attack of diphtheria the skin had become almost normal and the health was very good.

There seemed to be good ground for the assumption that this cutaneous phenomenon was due to the persistence of the epitrichial layer, which had preserved its integrity up to the time of birth, instead of being cast off by the seventh month, as in the normal fœtus. Whether this case was to be classified as a mild, attenuated form of the disease described as ichthyosis congenita or ichthyosis fœtalis, it was impossible for me to determine with the data at hand.

At a meeting of the Société de Dermatologie et de Syphiligraphie in January, 1892, Hallopeau and Watelet reported a case which they described as an attenuated form of the disease called fœtal ichthyosis. In this case the infant was seen by one of the reporters a quarter of an hour after birth, when the whole surface of the body was found to be covered with a white pellicle, so that one might have thought it thickly strewn with rice powder. Fifteen minutes later this pellicle became broken in places, especially at the flexures of the joints, and began to separate in large sheets. There was some ectropion. When this outer pellicle had been cast off, the skin beneath was seen to be reddened, and a mild exfoliation in the form of fine branny scales, unlike the large pieces that were formed by the breaking up of the pellicle, persisted for some time. The pellicle is compared to a layer of collodion that had been applied to the surface of the skin, and had broken at various points. The general condition of the infant was good.

This case was regarded by the reporters as an attenuated form of ichthyosis congenita, despite the marked difference from the severe cutaneous alterations that had previously been observed in this affection. Opinion was divided among the other members of the society, several, among them Besnier, declaring that if the conception of the term ichthyosis were properly held to, it would occur to no dermatologist to place this case under that heading.

At a later meeting of the society a letter from Kaposi was read, in which he calls attention to the plate in Hebra's atlas called ichthyosis sebacea, which seems to him analogous to the case described by Hallopeau, while the graver cases of ichthyosis congenita described by

Kyber, Hans Hebra, and others, he seems inclined to group by themselves.

In the *Annales de dermatologie et de syphiligraphie* for February, 1895, there appeared an interesting and suggestive article by Grass and Török upon a case of lamellated exfoliation of the newborn or the ichthyosis sebacea of Hebra. In this case the child, seen twenty-four hours after birth, looked as if covered with a thin layer of collodion, which was broken in places by fissures extending no deeper than the membrane itself. This covering was adherent in all parts except at the seat of the fissures, and here the skin deprived of the membrane appeared normal. The child died three days later from an intrameningeal hæmorrhage due to the application of the forceps.

Grass and Török, in their discussion of this case, assume its analogy to the ichthyosis sebacea as pictured by Hebra, and plead for the separation of these cases from the severe forms of diffuse keratoma described as ichthyosis congenita or fœtalis. Moreover, what is of especial interest, they refer to Welcker's epitrichium, or the distinct membrane covering the hairs of certain animals, and assume that in cases like their own and in all cases of "ichthyosis sebacea" the cells of the stratum corneum possess a greater coherence than usual, which results in the formation of an envelope completely analogous to the epitrichium of certain animals. This condition they regard as in no sense pathological; it is simply a variety of the physiological desquamation of the newborn.

Kaposi's view, that ichthyosis sebacea (which they assume to be the same condition as the case described by them) is caused by the sebaceous excretion continuing for a longer or shorter period after birth, and finally drying up and being cast off in the form of scales, is proved by microscopical examination to be erroneous, as no fat was found in bits of the membrane except at the mouths of the sebaceous glands. Ichthyosis congenita in the severe forms described by Kyber, Hebra, and in America by Elliot and Sherwell, they consider, as has been said, a totally distinct affection, as well as the ordinary ichthyosis. They propose to call the affection represented by their case "exfoliation lamelleuse des nouveau-nés," as in accord with the anatomical evolution of the process.

It seems to me that Grass and Török have done much toward clearing up this matter, and that in all probability different affections have been described as ichthyosis congenita. Whether all the cases called ichthyosis sebacea by the Vienna school are identical with Hallopeau's and Grass and Török's case it is impossible to say. Certainly the Hebra plate of ichthyosis sebacea is not inconsistent with such an as-

sumption. The prominence given to the seborrhœal element in such cases has added much to the confusion, as it is not shown that the scales and concretions are made up to any considerable extent of sebaceous matter—all the evidence points to the outer epidermal cells as solely responsible for the pathological condition.

Now, it can scarcely be questioned that the three cases just described—viz., Hallopeau's, Grass and Török's, and my own—represent the same pathological process. In all the child was born with a membranous covering which impressed the observers with its similarity to a layer of collodion or of oiled paper. After a short time this membrane began to peel off in large masses and sheets, leaving the normal skin below in a state of moderate desquamation, which slowly subsided. The health of these children was not visibly affected by the abnormality of the skin.

These three cases at least are to be grouped together, and are examples, in my opinion, of a persistence of the epitrichial layer, which has usually been cast off by the seventh fœtal month, but in these instances maintained its integrity up to the time of birth, when it enveloped the infants like a distinct membrane, such as is found in certain animals. Whether some of the other cases heretofore described under ichthyosis congenita may belong in this category and are due to the persistence of the epitrichial layer, it is difficult to form an opinion. There is the widest divergence in the clinical appearances found in the advanced cases of so-called congenital or fœtal ichthyosis and the three cases that I refer to. In these advanced cases of fœtal ichthyosis Kyber's name of universal diffuse keratoma seems justified. His histological studies showed a great proliferation of the cells of the rete and a correspondingly increased cornification of the upper cells, together with an enlargement of the interpapillary rete prolongations and of the sweat glands. Such cases can not certainly be explained by the persistence of a fœtal layer merely, but it may be that these outer cells are subject to pathological changes *in utero*, which play a part in the resulting deformity.

Grass and Török say that in all cases where the newborn child is covered with a horny layer, in process of slow detachment in large masses, we must assume a stronger coherence of the horny cells, which causes the formation of a horny envelope analogous to the epitrichium of certain animals. They consider this a variety of the physiological desquamation of the newborn and in no sense pathological. In other words, the membranous outer envelope is produced by a persistence of the scales of the horny layer proper, which are usually cast off gradually before and after birth.

It will be seen, from what has been said at the beginning of this article, that Grass and Török's view is probably not quite the true one, for it has been shown that there is in man an *epitrichial layer* which is at all times above and histologically different from the horny layer. As the epitrichial layer disappears by the seventh month, the normal desquamation of the last few months of fœtal life and of the newborn child is produced from the true horny layer. In the instances where the child is born with a covering or envelope composed of horny cells, as in the cases of Hallopeau, Grass and Török, and in my own, a rational explanation is that in these cases the epitrichial layer, instead of gradually exfoliating and disappearing by the seventh fœtal month, retains its integrity up to the time of birth, when the child is born covered with a membrane completely analogous to the epitrichium of some animals. Beneath this membrane lies the true horny layer which desquamates in small scales after its outer covering has been removed.